Pharmacologic Treatments in ADHD

Key Questions and Inclusion Criteria

Update #4

Key Questions

1. Evidence on Effectiveness and Efficacy
    a. What is the comparative or noncomparative evidence that pharmacologic treatments for attention deficit disorders improve *effectiveness* outcomes?
        i. Comparisons include individual drugs, as well as between stimulants and nonstimulants, and immediate release versus intermediate release versus long-acting formulations
        ii. Noncomparative evidence will be considered for drugs with no comparative evidence.
    b. What is the *comparative* efficacy between any included pharmacologic treatment, and between stimulants and nonstimulants, and between immediate release versus intermediate release versus long-acting formulations, for attention deficit disorders?
2. Tolerability, Serious Adverse Events, Misuse and Diversion
    a. What is the evidence of *comparative* tolerability of different pharmacologic treatments, and between stimulants and nonstimulants, and between immediate release versus intermediate release versus long-acting formulations, for attention deficit disorders?
    b. What is the evidence of serious adverse events or long-term adverse events associated with use of pharmacologic treatments for attention deficit disorders?
    c. What is the comparative or noncomparative evidence that pharmacologic treatments for attention deficit disorders impact the risk of misuse or illicit diversion in patients with no history of misuse or diversion?
        i. Comparisons include individual drugs, as well as between stimulants and nonstimulants, and immediate release versus intermediate release versus long-acting formulations
        ii. Noncomparative evidence will be considered for drugs with no comparative evidence.
3. Evidence in Subgroups of Patients
    a. What is the evidence of benefits and harms of pharmacologic treatments, and between stimulants and nonstimulants, and between immediate release versus intermediate release versus long-acting formulations, for attention deficit disorders in subgroups of patients based on demographics (age,

racial groups, gender), socioeconomic status, other medications or therapy, or co-morbidities (e.g. tics, anxiety, substance use disorders, disruptive behavior disorders)?

b. What is the comparative or noncomparative evidence of misuse or illicit diversion of pharmacologic treatments for attention deficit disorders in patients with current or past substance use disorder comorbidities?

    i. Comparisons include individual drugs, as well as between stimulants and nonstimulants, and immediate release versus intermediate release versus long-acting formulations

    ii. Noncomparative evidence will be considered for drugs with no comparative evidence.

Inclusion Criteria

Populations

Pediatric (aged < 3, < 6 yrs, and 6-17 years) and adult (aged ≥ 18 years) outpatients with Attention Deficit Disorders

- Attention Deficit Disorder
- Attention Deficit Hyperactivity Disorder

Treatments

Active Ingredients	Trade Name*	Forms
Amphetamine mixture (amphetamine aspartate; amphetamine sulfate; dextroamphetamine saccharate; dextroamphetamine sulfate)	Adderall*† Adderall XR	Oral tablet Extended release oral capsule
Atomoxetine HCl	Strattera	Oral capsule
Clonidine	Catapres, Catapres TTS*	Oral tablet, extended release transdermal film
	Kapvay	Extended release oral tablet
	Nexiclon	Extended release oral suspension and tablets
Dexmethylphenidate hydrochloride	Focalin*†	Oral tablet
	Focalin XR†	Extended release oral capsule
Dextroamphetamine sulfate	Dexedrine*	Oral tablet
	Dexedrine Spansule	Sustained release oral capsule
	Dextrostat*†	Oral tablet
	Liquadd	Oral solution
Guanfacine hydrochloride	Tenex*	Oral tablet
	Intuniv	Extended release oral tablet
Lisdexamfetamine dimesylate	Vyvanse†	Oral Capsule
Methamphetamine hydrochloride	Desoxyn†	Oral tablet
Methylphenidate hydrochloride	Concerta	Extended release oral tablet
	Daytrana†	Transdermal patch
	Metadate CD†	Extended release oral capsule
	Metadate ER†	Extended release oral tablet
	Methylin†	Oral chewable tablet Oral solution
	Ritalin*	Oral tablet
	Ritalin LA†	Extended release oral capsule
	Biphentin‡	Extended release oral capsule
	Ritalin SR	Extended release oral tablet
Modafinil	Provigil	Oral tablet
	Alertec‡	Oral tablet

*or generic equivalent
†Not available in Canada
‡Not available in the United States

Benefits

Effectiveness outcomes

1. Functional capacity (social, academic and occupational productivity)
2. Caregiver satisfaction (parent, teacher, other)
3. Quality of life (patient, family members, caregivers, teachers)
4. Time to onset of effectiveness
5. Duration of effectiveness (length of therapy)

Efficacy outcomes

1. Symptom response (inattention, hyperactivity-impulsivity, aggression, global ratings, etc.)

Harms

Tolerability

1. Overall adverse effect reports
2. Withdrawals due to adverse effects and overall withdrawal
3. Specific adverse events (insomnia, anorexia, abuse potential, tics, anxiety and sexual dysfunction)

Serious adverse effects

1. Hepatotoxicity
2. Cardiovascular events
3. Growth effects

Misuse/diversion

1. Trading, selling
2. Compliance, overdose
3. Development of substance abuse disorders

Study designs

- Effectiveness: Controlled clinical trials, good-quality systematic reviews, comparative observational studies (cohort studies including database studies, and case-control studies),
- Efficacy and general adverse events: Controlled clinical trials, good-quality systematic reviews
- Serious adverse events: Controlled clinical trials, good-quality systematic reviews, comparative observational studies (cohort studies including database studies, and case-control studies),
- Misuse/diversion: Controlled clinical trials, good-quality systematic reviews, comparative observational studies (cohort studies including database studies, and case-control studies), and noncomparative observational studies (before-after, time-series)
- Subgroups: Controlled clinical trials, good-quality systematic reviews, comparative observational studies (cohort studies including database studies, and case-control studies),